

We Claim:

1. Use of an acetylcholine esterase antagonist in the manufacture of a medicament useful in reducing insulin resistance in a mammalian patient suffering therefrom.
2. Use of an acetylcholine esterase antagonist in reducing insulin resistance in a mammalian patient suffering therefrom.
3. Use of any one of claims 1 or 2 wherein the insulin resistance is at least partially the result of inadequate levels of acetylcholine in the patient's hepatic parasympathetic nerve synapses.
4. Use of an acetylcholine esterase antagonist in the manufacture of a medicament useful to increase skeletal muscle glucose uptake in a mammalian patient.
5. Use of an acetylcholine esterase antagonist to increase skeletal muscle glucose uptake in a mammalian patient.
6. Use of claim 1, 2, 4 or 5 wherein the patient suffers from suboptimal hepatic regulation of blood glucose levels.
7. Use of claim 1, 2, 3, 4, 5 or 6 wherein the acetylcholine esterase antagonist is at least one of donepezil, galanthamine, rivastigme, tacrine, physostigmine, neostigmine, edrophonium, pyridostigmine, demecarium, pyridostigmine, phospholine, metrifonate, zanapezil, and ambenonium.
8. Use of any preceding claim wherein the patient is a human.
9. A pharmaceutical composition comprising a suitable acetylcholine esterase antagonist and at least one other drug used in the treatment of diabetes.

10. The composition of claim 9 further including a pharmaceutically acceptable liver-targeting substance.

11. The composition of claim 9 or 10 wherein the antagonist is at least one of donepezil, galanthamine, rivastigme, tacrine, physostigme, neostigmine, edrophonium, pyridostigmine, demecarium, pyridostigmine, phospholine, metrifonate, zanapezil, and ambenonium.

12. The composition of claim 9, 10 or 11 wherein the other drug is at least one of insulin, insulin analogues, sulfonylurea agents, tolbutamide, acetohexamide, tolazamide, chlorpropamide, glyburide, glipizide, glimepiride, biguanide agents, metformin, alpha-glucosidase inhibitors, acarbose, miglitol, thiazolidinedione agents (insulin sensitizers), rosiglitazone, pioglitazone, troglitazone, meglitinide agents, repaglinide, phosphodiesterase inhibitors, anagrelide, tadalafil, dipyridamole, dyphylline, vardenafil, cilostazol, milrinone, theophylline, sildenafil, caffeine, cholinergic agonists, acetylcholine, methacholine, bethanechol, carbachol, pilocarpine hydrochloride, nitric oxide donors, products or processes to increase NO synthesis in the liver, SIN-1, molsidamine, nitrosylated N-acetylcysteine, nitrosylated cysteine esters, nitrosylated L-2-oxothiazolidine-4-carboxylate (OTC), nitrosylated gamma glutamylcystein and its ethyl ester, nitrosylated glutathione ethyl ester, nitrosylated glutathione isopropyl ester, nitrosylated lipoic acid, nitrosylated cysteine, nitrosylated cystine, nitrosylated methionine, S-adenosylmethionine, products or processes to reduce the rate of NO degradation in the liver, products or processes to provide exogenous NO or an exogenous carrier or precursor which is taken up and releases NO in the liver, antioxidants, vitamin E, vitamin C, 3-morpholinobutylamine, glutathione increasing compounds, N-acetylcysteine, cysteine esters, L-2-oxothiazolidine-4-carboxylate (OTC), gamma glutamylcystein and its ethyl ester, glutathione ethyl ester, glutathione isopropyl ester, lipoic acid, cysteine, cystine, methionine, and S-adenosylmethionine.

13. The composition of claim 10, 11 or 12 wherein the liver-targeting substance is at least one of albumin, bile salts and liposomes.
14. A kit comprising:
an acetylcholine esterase antagonist in a pharmaceutically acceptable carrier; and
instructions for the administration of the acetylcholine esterase antagonist to reduce insulin resistance in a mammalian patient.
15. The kit of claim 14 further comprising means to administer the acetylcholine esterase antagonist.
16. A method of reducing insulin resistance in a mammalian patient comprising administering a suitable acetylcholine esterase antagonist.
17. A method of amplifying the effect of the hepatic parasympathetic reflex on skeletal muscle insulin sensitivity comprising administering an acetylcholine esterase antagonist.
18. A method of increasing glucose uptake by skeletal muscle of a patient suffering from suboptimal hepatic regulation of blood glucose levels, comprising identifying the patient as suffering from suboptimal hepatic regulation of blood glucose levels and administering a suitable acetylcholine esterase antagonist.
19. A method of reducing insulin resistance in a mammalian patient suffering from inadequate levels of acetylcholine in the hepatic parasympathetic nerve synapses, said method comprising identifying the patient as suffering from inadequate levels of acetylcholine in the hepatic parasympathetic nerve synapses and administering a suitable acetylcholine esterase antagonist.
20. The method of any preceding claim wherein the acetylcholine esterase antagonist is at least one of donepezil, galanthamine, rivastigme,

tacrine, physostigmine, neostigmine, edrophonium, pyridostigmine, demecarium, pyridostigmine, phospholine, metrifonate, zanapezil, and ambenonium.

21. The method of any preceding claim wherein the acetylcholine esterase antagonist is targeted to the liver.

22. The method of claim 21 wherein the acetylcholine esterase is targeted to the liver using albumin.

23. The method of claim 21 wherein the acetylcholine esterase is targeted to the liver using a plurality of liposomes.

24. The method of claim 21 wherein the acetylcholine esterase is targeted to the liver using bile salts.

25. The method of any preceding claim wherein the acetylcholine esterase is administered by intravenous administration.

26. The method of any preceding claim wherein the acetylcholine esterase is administered by transdermal administration.

27. The method of any preceding claim wherein the acetylcholine esterase is administered by oral administration.

28. The method of any preceding claim wherein the acetylcholine esterase is administered by intra peritoneal administration.

29. The method of any preceding claim wherein the acetylcholine esterase antagonist is administered by portal vein injection.

30. The method of any preceding claim wherein the acetylcholine esterase antagonist is administered by immobilization of the acetylcholine

esterase antagonist on a solid support and implantation of the support adjacent the patient's liver.

31. The method of any preceding claim wherein the patient suffers from at least one of chronic liver disease, chronic hypertension, type II diabetes, fetal alcohol syndrome, gestational diabetes, age-related insulin resistance, and hepatic nerve damage.

32. The method of any preceding claim wherein the patient is a human.

33. Use of claim 1, 2 or 3 wherein the insulin resistance is hepatic insulin sensitizing substance-dependent insulin resistance.

34. The method of any preceding claim wherein the insulin resistance is hepatic insulin sensitizing substance-dependent insulin resistance.